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Reversible splenial lesion syndrome (RESLES) associated with NMDAR antibody type autoimmune encephalitis

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Abstract

Reversible splenial lesion syndrome (RESLES) is frequently observed in encephalitis or encephalopathy caused by various pathogens such as influenza virus A, rotavirus, and measles. It is also associated with epileptic seizures, anti-epileptic drug withdrawal and neuroleptic malignant syndrome. We report here a Sri Lankan woman with RESLES associated with anti-NMDAR antibody encephalitis and neuroleptic malignant syndrome.

Keywords: Reversible splenial lesion syndrome (RESLES), NMDAR antibody encephalitis, neuroleptic malignant syndrome (NMS).

INTRODUCTION

Reversible splenial lesion syndrome (RESLES) is a rare clinico-radiological entity.[1] It is characterized by a reversible lesion in the splenium of the corpus callosum (SCC) seen on MRI. It can develop in association with seizures and/or anti epileptic drug withdrawal, alcohol, trauma and CNS infections. Reversible demyelination due to anti-epileptic drug toxicity, and trans callosal spread of secondary generalized seizures causing edema are possible reasons why RESLES is most common in epilepsy.[1] RESLES is only rarely reported in autoimmune encephalitis.[2] MRI findings include an oval or semi-oval signal increase in the SCC (boomerang sign) in T2 and FLAIR with diffusion restriction without contrast enhancement.[1,2] Reversible signal changes on DWI and ADC are identified in all patients. Complete resolution of MRI findings in weeks or months is typical. Rarely neuroleptic malignant syndrome (NMS), which our patient developed is also associated with RESLES. We report here a young Sri Lankan woman with anti-NMDAR antibody encephalitis, NMS and RESLES.

CASE REPORT

A 29-year old Sri Lankan woman presented with an altered level of consciousness and behavioral abnormalities. She was erratic and irrational in her behavior from two weeks prior to this admission. She was forgetful and was verbalizing inappropriately. A short course of neuroleptics has been administered for her symptoms by her GP. This worsened the condition leading to generalize rigidity and fever. There were no witnessed seizures. Deep tendon reflexes were normal with down going plantar. Haematology showed a neutrophil leukocytosis and high CPK >7000 U/L. Her basic CSF findings were normal. EEG was generally slow without epileptiform discharges. NMDAR antibody in the CSF was positive. MR scan of brain was unremarkable other than for the TI hypo intensity and T2 and Flair hyper intensity without contrast enhancement in SCC. (Figure 1A). She responded well to immune suppression with IV methyl prednisolone and plasma exchange. Abdominal ultrasound revealed an ovarian teratoma which was surgically removed. (Figure 1 C, D, E). Co-morbidity of NMS was treated with dantrolene Sodium and supportive therapy. Repeat MRI one month later showed complete resolution of the SCC lesion. (Figure 1B).

DISCUSSION

RESLES is most often identified in patients with seizures and/or anti-epileptic drug withdrawal[3], however, it is also frequently observed in encephalitis or encephalopathy caused by various pathogens such as influenza virus A,

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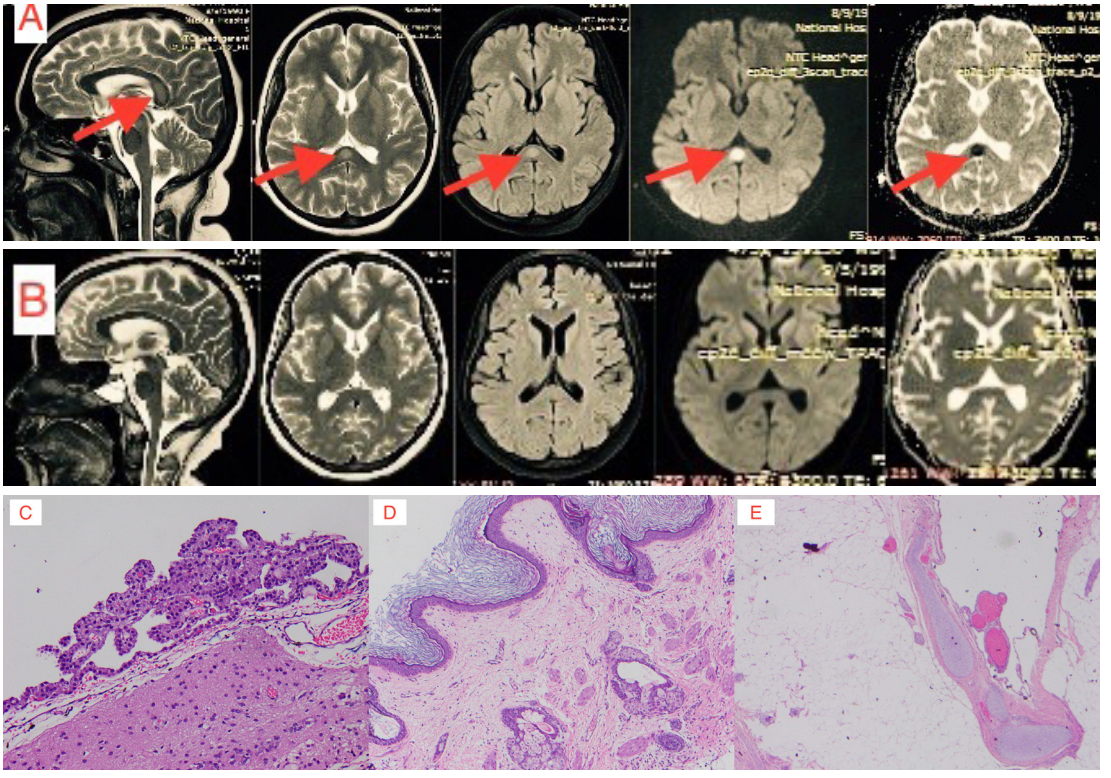

Figure 1. (**A**) Pre-treatment: MRI imaging of the brain of sagittal and axial T2, FLAIR, DWI hyperintensities and corresponding ADC map hypointensity shows an ovoid lesion at the centre of the splenium of the corpus callosum (SCC) — hyperintense on FLAIR with markedly restricted diffusion and decreased ADC values. (Boomerang sign). (Red arrow). (**B**) Follow up MRI performed 4 weeks after: sagittal and axial T2. The pathological examination revealed the presence of (**C**) glial and choroid plexus, (**D**) skin and adnexa, and (**E**) cartilage tissues in teratoma.

rotavirus, measles, herpesvirus 6, adenovirus, mumps, Epstein-Barr virus and *Escherischia coli*, and others. (Table 1, 2)[1,3] Corpus callosum is generally resistant to ischemia. The exact pathophysiological explanations for an isolated lesion in selenium of corpus callosum is still

Table 1: Encephalitic RESLES

ENCEPHALITIC AETIOLOGIES OF 'RESLES'
VIRAL
Rota virus
influenza A & B
Varizella -zoster
Adenovirus
Herpesvirus -6
Epstein-Barr virus
BACTERIAL
E-coli 0157
Salmonella enteritidis.
Legionella pneumoniae
Mycoplasma pneumoniae
NON INFECTIVE - AUTOIMMUNE
Autoimmune Encephalitis – e.g. NMDAR antibody encephalitis

Table 2: Non encephalitic RESLES.

NON ENCEPHALITIC AETIOLOGIES OF 'RESLES'	
EPILEPSY *related.*	*and anti-epileptic drugs withdrawal******
****** Seizures alone and without clinical seizures however while on anti-epileptic drugs were also reported.*	
METABOLIC	*Hypoglycemia and hyperglycemia* *Hypernatremia.*
High altitude pulmonary edema	
Malnutrition/ anorexia nervosa	
Marchiafava-Bignami disease	
Vitamin B12 deficiency	
SLE	
DRUGS	*methyl bromide exposure* *Cisplatinum and 5- FU* *5-FU* *Carboplatin* *Olanzapine and Citalopram*

unclear. Cytotoxic edema is likely the most plausible explanation. The reports of RESLES is uncommon in confirmed cases of autoimmune encephalitis. After the first report in literature of RESLES in NMDAR antibody encephalitis in 2015 ours is probably only the second case.[2] This is an extremely rare association. The neurological symptoms of RESLES associated with encephalitis usually has a complete recovery without residual neurological sequelae after a short disease course. Most patients with RESLES associated with encephalitis/encephalopathy were reported in Japanese population.[4] In autoimmune encephalitis initial neuropsychiatric symptoms are common. Use of neuroleptics in them could lead to life threatening NMS. NMS also could be rarely associated with RESLES but with good outcomes. RESLES associated with encephalitis has a good prognosis. We find in the limited number of cases in literature of RESLES with encephalitis most improve with treatment of the underlying condition. Hence we postulate that immunotherapy with removal of the teratoma would have been the most likely reason for her complete recovery with radiological resolution. However a few patients might have severe neurological sequelae. Reversible signal changes on DWI and ADC are identified in all patients. Repeat MR scan of brain in one month will confirm the diagnosis of RESLES. In our patient in addition to confirmed NMDAR antibody encephalitis with an ovarian teratoma the coexistence of NMS may have contributed in its causation.

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